COMPARATIVE SAFETY OF TOCILIZUMAB VERSUS OTHER BIOLOGIC DMARDS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A LARGE MULTI-DATABASE COHORT STUDY

Final Study Report

October 17, 2018

Roche Study # MA39102

STUDY SUMMARY - ABSTRACT

Aim 1-

Objectives: To examine the rate of incident malignancy excluding non-melanoma skin cancer (NMSC) in patients with rheumatoid arthritis (RA) newly treated with tocilizumab versus other biologic drugs.

Methods: We conducted a cohort study using data from 3 U.S. insurance claims databases – Medicare (2010-15), 'IMS' PharMetrics Plus (2011-2015) and Truven 'MarketScan' (2011-2015). Adult patients with RA who newly started tocilizumab or a TNF inhibitor (TNFi) after failing a different TNFi, abatacept or tofacitinib were included. The primary outcome was incident malignancy excluding NMSC. To control for confounding, tocilizumab starters were propensity score (PS)-matched to TNFi starters with a variable ratio of 1:3 within each database. Hazard ratios (HR) from the 3 PS-matched cohorts were combined by an inverse variance-weighted, fixed-effects model. We also conducted a secondary analysis where we compared tocilizumab starters with abatacept starters.

Results: We included 13,102 tocilizumab initiators PS-matched to 26,727 TNFi initiators in all three databases. The IR of malignancy per 1,000 person-years ranged from 8.27 (IMS) to 23.18 (Medicare) in the tocilizumab group and from 9.64 (MarketScan) to 21.46 (Medicare) in the TNFi group. The risk of incident malignancy was similar between the two groups across all three databases, with a combined HR of 0.98 (95%CI 0.80-1.19) in tocilizumab versus TNFi initiators. The secondary analysis comparing tocilizumab versus abatacept showed similar results (combined HR 0.97, 95%CI 0.74-1.27).

Conclusions: This large multi-database cohort study found no difference in the risk of malignancy excluding NMSC in patients with RA who newly started tocilizumab compared with TNFi or abatacept.

Aim 2-

Objectives: While biologics are known to be associated with risk of serious infections, data on head-to-head comparison of different biologic drugs for the risk of infection are limited. We aimed to investigate the rate of incident serious bacterial, viral or opportunistic infection in (RA) patients starting TCZ versus TNFi.

Methods: We conducted a cohort study using data from 3 U.S. healthcare claims databases: Medicare (2010-2015), 'IMS' PharMetrics Plus (2011-2015) and Truven 'MarketScan' (2011-2015). We identified patients with RA aged≥18 years who initiated TCZ or a TNFi with prior use of at least one different TNFi, abatacept or tofacitinib. Patients with recent infection, malignancy or rituximab use were excluded. The primary endpoint was incident composite serious infection including bacterial, viral or opportunistic infection with ≥1 inpatient principal diagnosis code. Secondary outcomes were specific subtypes of serious infection. To control for >70 potential confounders including demographics, prior DMARD and antibiotic use, comorbidities, medications, and healthcare utilization in each database, TCZ initiators were propensity score (PS)-matched to TNFi initiators with a variable ratio of 1:3 within each database. We then calculated incidence rates (IR) and hazard ratios (HR) of the primary and secondary outcomes in each database.

Results: A total of 16,074 TCZ initiators were PS-matched to 33,109 TNFi initiators. Mean age was 72 years in Medicare, 51 in IMS and 53 in MarketScan. At baseline, 69-73% patients used methotrexate and 70-79% used corticosteroids. In the as-treated analysis, the median follow-up time (days) ranged from 181 (MarketScan) to 213 (IMS) in the TCZ group and 198 (Medicare) to 235 (IMS) in the TNFi group. A total of 618 serious infections occurred in TCZ and 1,155 in TNFi group across the three databases. In the TCZ group, the IR for serious infections per 1000 person-years ranged from 3.07 (MarketScan) to 7.05 (Medicare), and in the TNFi group, it ranged from 2.47 (MarketScan) to 7.05 (Medicare). The risk of incident composite serious infections was similar in TCZ versus TNFi initiators with a combined HR of 1.05 (95%CI 0.95-1.16) across all three databases. However, TCZ was associated with an increased risk of serious bacterial infection (HR 1.19, 95% CI 1.07-1.33), skin and soft tissue infections (HR 2.38, 95% CI 1.47-3.86) and diverticulitis (HR 2.34, 95% CI 1.64-3.34) compared to TNFi initiators. Secondary and subgroup analyses showed similar results**.**

Conclusions: This large multi-database cohort study found no difference in the risk for the composite primary endpoint of serious infection requiring hospitalization in RA patients who initiated TCZ versus TNFi after failing ≥1 biologic drug or tofacitinib. However, the risk of serious bacterial infection, skin and soft tissue infections, and diverticulitis was higher in TCZ initiators versus TNFi.